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Effects of Curcumin in Workers with Noise-Induced Hearing Loss: Preliminary Report

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Abstract

Introduction:

Prolonged loud noise exposure causes sensorineural hearing loss through cochlear oxidative stress, requiring heat shock protein 70 (HSP70) for protection. Curcumin boosts antioxidant expression and safeguards the cochlea. Pure tone audiometry (PTA) measures the type of hearing loss and otoacoustic emission (OAE) detects early auditory issues. This study evaluated the impact of Curcumin on noise-exposed workers via PTA, OAE, and HSP70.

Materials and Methods:

This preliminary study included 54 noise-exposed workers with hearing thresholds ≥26 dB and SNR values <6 dB. Participants were randomized into three noise-exposed groups: placebo (positive control), 500 mg Curcumin, or 1,000 mg Curcumin for 4 weeks. A negative control group of 18 non-exposed workers with normal hearing who received no treatment, served as an external reference only. HSP70 levels, PTA, and OAE were measured before and after intervention in all groups.

Results:

PTA showed a significant worsening of hearing threshold in the positive control group (p=0.001), significant improvement in Curcumin 500 mg group (p=0.046), in the Curcumin 1,000 mg (p=0.059). OAE revealed substantial worsening of SNR in the positive control group (p<0.001) and significant increase in the Curcumin 500 mg (p<0.05) at 4, 7, 8, and 9 kHz, and in the 1,000 mg groups (p<0.05) at 5, 8, and 9 kHz. HSP70 levels significantly increased in the positive control group (p=0.021), both Curcumin groups showed a non-significant increase.

Conclusion:

Curcumin was associated with improved hearing thresholds and favorable SNR changes in noise-exposed workers. Changes in HSP70 levels were minimal and not statistically significant in the curcumin groups.

Keywords: Curcumin, Heat Shock Protein 70, Noise-Induced Hearing Loss, Pure Tone Audiometry, Otoacoustic Emission

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Introduction

Globally, 16% of hearing impairments in adults are attributed to Noise-Induced Hearing Loss (NIHL) (1). The World Health Organization (WHO) reports that one in ten people worldwide are subjected to hazardous noise levels. Prolonged exposure to loud sounds causes half of all hearing loss cases worldwide (2). Research at Dr. Soetomo General Hospital in Surabaya, revealed that 47.92% of workers experienced NIHL with noise levels between 85.39 and 112.90 dB (3). A study at the Begerpang Palm Oil Mill in North Sumatra found that 35% of employees had NIHL, with noise exposure ranging from 60 to 94.5 dB (4).

Prolonged exposure to loud sounds damages the cochlea, disrupts blood circulation, triggers inflammation, oxidative stress, and overstimulates hair cells and nerves, leading to excitotoxicity and predominantly apoptotic death of hair cells (5).

Heightened mitochondrial respiration, ischemia and reperfusion from noise exposure generate reactive oxygen species (ROS) levels surpass neutralization capacity, causing hair cell death via apoptosis or necrosis. ROS formation induces proinflammatory cytokine production, exacerbating damage (6).

The cochlea defends against noise by expressing heat shock protein 70 (HSP70), which protects hair cells from apoptotic stress in the inner ear (7,8). HSP70, which also appears in plasma as extracellular HSP70, may serve as a biomarker for diseases associated with low-grade inflammation (9).

HSP70 levels in the blood and Organ of Corti were elevated in Rattus norvegicus exposed to loud noise, suggesting a protective role against noise-induced damage in the inner ear (10).

Pure tone audiometry (PTA) can assess hearing impairment but cannot detect early-stage impairments. Otoacoustic emission (OAE) test identifies noise-exposed workers at risk of NIHL (11). Hearing loss treatment is challenging (12). Research has shown that certain dietary supplements protect cochlear neural stem cells from age-related and noise-induced damage (13). Curcumin (*Curcuma longa*) has antioxidant, antimutagenic, anti-inflammatory, and antimicrobial properties (14). Animal research demonstrated that curcumin treatment enhanced cochlear function in rats with noise-induced trauma, as indicated by improved signal-to-noise ratio (SNR) measurements (15).

Limited research exists on the effects of curcumin on the human cochlea after noise exposure. This study evaluated the effect of curcumin on hearing in noise-exposed workers using PTA, OAE, and HSP70 blood levels.

Materials and Methods

This preliminary report employed a double-blind randomized controlled trial design with pretest and posttest data analysis was conducted on 54 workers who met the inclusion criteria, approved by Universitas Sumatera Utara Health Research Ethical Committee Number 810/KEP/USU/2021, and includes informed consent from all participants. The noise-exposed workers were randomly assigned to the placebo (positive control), 500 mg Curcumin, and 1,000 mg Curcumin groups using block randomization. The negative control group, which was not exposed to noise and Curcumin, consisted of 18 participants. Randomization and double-blinding procedures were implemented only in the three noise-exposed groups. Due to the nature of the intervention, blinding was not feasible for the negative control group, which was included solely to provide external references values for baseline comparison. In total, the study comprised 72 samples.

Sample

The study, conducted at the Laundry and Nutrition Installations of Adam Malik Hospital and an Iron Factory in Medan City, determined the sample size using the Federer formula, requiring at least 6 individuals per group across 4 groups, and employed consecutive sampling to include all eligible participants. Workers were exposed to noise levels >85 dB for 8 hours daily, 40 hours weekly, and met the inclusion criteria of sensorineural hearing loss in pure tone audiometry with hearing threshold greater or equal to 26 dB and SNR < 6 dB, over 5 years of employment in noisy areas, no ear or upper respiratory infections, no tympanic membrane perforation, hypertension, Diabetes Mellitus, no ototoxic drug consumption, and provision of informed consent.

Noncompliance with curcumin consumption was the exclusion criterion. In the negative control group, workers were not exposed to noise and had a hearing threshold of < 26 dB

and an SNR ≥ 6 dB. The negative control group was included to determine the levels of HSP70 in workers who were not exposed to noise and had normal hearing thresholds and SNR values.

Procedure

Workers avoided noise exposure for at least 14 hours before examinations in a soundproof room (16). PTA used a calibrated Interacoustic Type AA222 Diagnostics audiometer (Denmark). Air conduction testing was performed using headphones at frequencies of 0.25, 0.5, 1, 2, 4, and 8 kHz.

Subsequently, bone conduction testing was conducted using a vibrator placed on the mastoid bone at frequencies of 0.25, 0.5, 1, 2, and 4 kHz to identify sensorineural, conductive, or mixed hearing loss. According to the World Health Organization (WHO) criteria, normal hearing is defined as an average hearing threshold of 0.5, 1, 2, and 4 kHz at ≤ 25 dB, whereas hearing loss is diagnosed when the threshold is equal to or greater than 26 dB. OAE testing was conducted using a calibrated Grason-Stadler Corti system (USA). The type of OAE measured was the distortion product otoacoustic emission (DPOAE), at test frequencies of 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 kHz. The initial stimulus frequency ratio was set at f1: f2 = 1.22, with stimulus intensities of L1/L2 = 65/55 dB. The results were considered a pass when the signal-to-noise ratio (SNR) was equal to or greater than 6 dB. OAE used a calibrated Grason-Stadler Corti (USA).

The OAE type was distortion product otoacoustic emission (DPOAE) with the frequency tested were 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 kHz, with an initial stimulus frequency of fi: f2=1.22 and an initial stimulus intensity of L1/L2 = 65/55 dB. The result was considered a pass if the signal-to-noise ratio (SNR) ≥ 6 dB. After confirming NIHL via PTA and OAE, a 3 ml blood sample was taken from the cubital vein, placed in an EDTA blood tube, and stored in a cooler box at 2°C-8°C.

The specimen was centrifuged at 1,000xg for 15 minutes and stored at −20°C. Workers who met the inclusion criteria were allocated to positive control group, 500 mg Curcumin group, and 1,000 mg Curcumin group.

The positive control group comprised participants continuously exposed to noise and administered a placebo (noise exposure and no curcumin), whereas the negative control group comprised participants unexposed to noise (no noise exposure and no curcumin). Capsules containing curcumin extract (turmeric extract, curcuma longa) standardized using High-Performance Liquid Chromatography (HPLC) with a concentration of 0.028% w/w ± 1.38% in 500 mg capsules.

The positive control group received a placebo. The 500 mg curcumin group was administered capsules containing 500 mg of curcumin, whereas the 1,000 mg group received two capsules containing 500 mg of curcumin each. All groups consumed the assigned capsules daily for a duration of four weeks. Hearing function was assessed using PTA and OAE, and blood samples were collected post-treatment. HSP70 levels were analyzed at the Laboratorium Terpadu, Faculty of Medicine, Universitas Sumatera Utara, using an ABclonal HSP70 ELISA Kit (Catalog No. RK07682). A 450 nm wave spectrophotometric examination was performed using Thermo Scientific (Multiskan Go, Finland) to determine HSP70 blood levels. Weekly checklists were reviewed and capsule counts were performed at follow-up to monitor compliance. Participants who consumed of ≥ 80% of the prescribed dosage were considered adherent.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) was used to analyze the data. Shapiro-Wilk test will be used to assess data normality. One-way ANOVA will be used for bivariate analysis if the data are normally distributed; otherwise, the Kruskal-Walli's test will be used. Subsequently, either the post-hoc Bonferroni test or the Mann-Whitney test will be conducted, depending on data normality. Data following a normal distribution were presented as mean values, whereas non-normally distributed data were expressed as median values.

Results

This study included 72 participants divided into four groups of 18 participants each.

Table 1. The Demographic Characteristics of the Research Participants

Demographics Characteristic	Positive Control	Curcumin 500 mg	Curcumin 1,000 mg	Negative Control
Gender, n (%)				
Male	16 (88,9)	15 (83,3)	16 (88,9)	7 (38,9)
Female	2 (11,1)	3 (16,7)	2 (11,1)	11 (61,1)
Age, year				
Mean (SD)	37,11 (6,04)	37,61 (5,75)	37,78 (6,41)	34 (3,71)
Length of working, year				
Mean (SD)	13,17 (3,57)	12,89 (4,63)	12,17 (3,5)	15,56 (4,05)

SD: Standard Deviation

Table 1 showed the male predominance in all three groups. The mean age was 37 years, and the average employment duration exceeded 12 years in all four groups.

Table 2 showed a significant improvement in hearing threshold for Curcumin 500 mg group (p=0.046).

Table 3 showed the positive control group had the highest delta hearing threshold, with a mean deterioration of 1.11 dB (p <0.001).

Table 2. Primary outcome of Hearing Tresshold (PTA average of 0.5, 1, 2, and 4 kHz in the better ear at baseline) Before and After Treatment

Group	Before Treatment		After Treatment		p
	Hearing tresholds, dB	95% Confidence Interval	Hearing tresholds, dB	95% Confidence Interval	
Positive control	32.3 (5.62)	29.49-35.08	33.4 (5.12)	30.85-35.95	0.001[a]
Curcumin 500 mg	32.85 (4.73)	30.49-35.2	32.49 (4.74)	30.13-34.84	0.046[b]
Curcumin 1,000 mg	32.80 (4.02)	30.08-34.08	31.73 (4.04)	29.72-33.74	0.059[a]
Negative control	18.26 (3.1)	16.72-19.8	18.54 (2.62)	17.24-19.84	0.409[b]

Data were presented as mean (SD) [a]Wilcoxon, [b] T Dependent

Table 3. The Differences in Changes in Hearing Threshold Before and After Treatment

Group	Delta in Hearing Treshold, dB	95% Confidence Interval	p	Posthoc		
				Curcumin 500 mg	Curcumin 1,000 mg	Negative control
Positive control	-1.11 (0.94)	-1.58- -0.63	<0.001[a]	0.019	0.044	0.57
Curcumin 500 mg	0.36 (0.71)	0.006 - 0.715			1	1
Curcumin 1,000 mg	0.34 (0.71)	-0.009 - 0.704				1
Negative control	-0.27 (1.39)	-097 - 0.41				

Data were presented as mean (SD) [a]Kruskal Wallis

Table 4. The Differences in SNR Values Before and After Treatment

Frequency	Group	Before Treatment		After Treatment		p
		SNR, dB	95% Confidence Interval	SNR, dB	95% CI	
1.5 kHz	Positive control	25 (4.1)	22.96-27.04	7(-17-16)	1.09-9.24	<0.001[a]
	Curcumin 500 mg	25 (2-31)	18.51-27.16	9.5 (-15-19)	4.16-11.95	<0.001[a]
	Curcumin 1,000 mg	25(2-31)	18.79-26.54	10.44 (4.54)	8.19-12.70	<0.001[a]
	Negative control	13.67 (6.53)	10.41-16.93	19.5 (14-31)	17.14-22.20	0.003[a]
2 kHz	Positive control	26.5(-7-32)	20.53-29.35	-1.06 (6.67)	-4.37-2.26	<0.001[a]
	Curcumin 500 mg	26.5 (-15-31)	13.42-26.58	5.5(2 - 14)	-4.19-7.81	0.002[a]
	Curcumin 1,000 mg	28.5(4 – 32)	23.51-29.71	5.78 (5.59)	3.00-8.56	<0.001[a]
	Negative control	14.83 (5.06)	12.32-17.35	21.23 (6.19)	18.25-24.41	0.001[b]
3 kHz	Positive control	6.94 (6.07)	3.92-9.96	-0.72 (3.98)	-2.70-1.26	<0.001[b]
	Curcumin 500 mg	6.33 (5.49)	3.60-9.06	5.33 (4.89)	2.90-7.76	0.532[b]
	Curcumin 1,000 mg	4.5 (-12 – 14)	2.10-7.35	3.83 (4.16)	1.76-5.90	0.254[a]
	Negative control	18.5(5 – 25)	14.14-20.86	16.56 (5.75)	13.70-19.42	0.623[a]
4 kHz	Positive control	-0.06 (4.02)	-2.06-1.94	-1.17 (6.25)	-4.28-1.94	0.585[b]
	Curcumin 500 mg	0(-8 – 4)	-2.54-0.54	1.28 (2.72)	-0.07-2.63	0.013[a]
	Curcumin 1,000 mg	-0.11 (3.25)	-1.73-1.51	1.83 (3.63)	0.03-3.64	0.121[b]
	Negative control	18.78 (6.59)	15.50-22.05	18(7 - 24)	13.72-19.06	0.378[a]
5 kHz	Positive control	4.28 (3.32)	2.63-5.93	0.5 (5.85)	-2.41-3.41	0.057[b]
	Curcumin 500 mg	1.94 (4.08)	-0.08-3.97	3.17 (4.42)	0.97-5.37	0.290[b]
	Curcumin 1,000 mg	2.33 (2.79)	0.95-3.72	5.06 (3.64)	3.25-6.86	0.016[b]
	Negative control	15 (3 – 24)	12.08-19.59	19.61 (6.58)	16.34-22.88	0.064[a]
6 kHz	Positive control	11.06 (5.69)	8.22-13.89	-0.44 (5.10)	-2.98-2.09	<0.001[b]
	Curcumin 500 mg	6.5(0 – 21)	5.46-11.65	4.8 (3.88)	2.90-6.76	0.118[a]
	Curcumin 1,000 mg	7.44 (4.94)	4.99-9.90	5.11 (4.36)	2.94-7.28	0.062[b]
	Negative control	18.5 (3.85)	16.58-20.42	19.89 (4.64)	17.58-22.20	0.449[b]
7 kHz	Positive control	14.11 (5.55)	11.35-16.87	5.17 (7.71)	1.33-9.00	<0.001[b]
	Curcumin 500 mg	10.61 (5.1)	8.07-13.15	15.44 (4.06)	13.42-17.46	0.009[b]
	Curcumin 1,000 mg	11.72 (5.19)	9.14-14.30	13.56 (5.76)	10.69-16.42	0.330[b]
	Negative control	18.56 (5.34)	15.90-21.21	21.5(1 – 27)	15.8-22.98	0.689[a]
8 kHz	Positive control	13.89 (6.23)	10.79-16.99	8.83 (8.24)	4.74-12.93	0.016[b]
	Curcumin 500 mg	10.5(6 – 24)	9.03-13.19	18.17 (4.53)	15.92-20.42	<0.001[b]
	Curcumin 1,000 mg	12.33 (3.9)	10.40-14.27	20.5(6 – 23)	16.32-20.79	0.003[a]
	Negative control	23(14 – 26)	19.22-23.45	22.28 (4.08)	20.25-24.31	0.646[a]
9 kHz	Positive control	14.5(11 – 26)	14.51-19.60	17.56 (7.22)	13.96-21.15	0.887[a]
	Curcumin 500 mg	13.28 (3.77)	11.40-15.15	22.5(-8 – 27)	14.55-24.34	0.031[a]
	Curcumin 1,000 mg	13(8 – 22)	11.12-14.32	23.61 (3.6)	21.82-25.40	<0.001[a]
	Negative control	20.61 (614)	17.56-23.66	16(0 – 21)	10.47-16.53	0.003[a]
10 kHz	Positive control	26.17 (3.99)	24.18-28.15	14(-1 – 22)	10.32-17.46	<0.001[a]
	Curcumin 500 mg	22.28 (6.63)	18.98-25.58	20(6 – 25)	16.57-20.87	0.062[a]
	Curcumin 1,000 mg	26(14 – 28)	22.47-26.31	19.17 (4.09)	17.13-21.20	0.002[a]
	Negative control	24.67 (6.8)	21.29-28.05	17.5(0 – 27)	13.39-20.06	0.005[a]
11 kHz	Positive control	26.33 (3.09)	24.80-27.87	12(-7 – 19)	6.08-13.70	<0.001[a]
	Curcumin 500 mg	23(1 – 29)	14.92-23.19	12.44 (4.85)	10.03-14.86	0.011[a]
	Curcumin 1,000 mg	23(9 – 30)	19.55-25.45	14(2 – 20)	11.04-15.52	<0.001[a]
	Negative control	23 (3.36)	21.33-24.67	11.83 (6.11)	8.80-14.87	<0.001[b]
12 kHz	Positive control	22 (3.16)	20.43-23.57	1.22 (3.42)	-0.48-2.92	<0.001[b]
	Curcumin 500 mg	17(-4 – 23)	9.47-17.98	2.5(0 – 11)	2.13-5.76	0.001[a]
	Curcumin 1,000 mg	20.5(-5 – 23)	13.21-21.24	2(-1 – 16)	1.45-6.44	<0.001[a]
	Negative control	24.83 (5.21)	22.25-27.42	13.61 (9.12)	9.08-18.14	<0.001[b]

Data were presented as mean (SD), median (min – max) [a]*Wilcoxon,* [b] *T Dependent*

Table 4 showed a significant worsening in SNR values in the positive control group at 1.5, 2, 3, 6, 7, 10, 11, and 12 kHz frequencies between pre- and post-treatment ($p<0.001$). The Curcumin 500 mg group had a significant increase in SNR values at 4, 7, 8, and 9 kHz ($p<0.05$), with a non-significant increase at 5 kHz ($p>0.05$). The Curcumin 1,000 mg group showed significant increase at 5, 8, and 9 kHz ($p<0.05$), and a non-significant increase at 4 and 7 kHz ($p>0.05$). A significant increase was observed at 1.5 and 2 kHz ($p<0.05$), and a non-significant increase at 5, 6, and 7 kHz ($p>0.05$) in the negative control group.

Table 5. The Differences in The Changes SNR Before and After Treatment

Frequency	Group	Delta SNR	95% Confidence Interval	P	Posthoc		
					Curcumin 500mg	Curcumin 1,000 mg	Negative control
1.5 kHz	Positive control	-19.83 (8.68)	-24.14--15.51	<0.001[a]	0.047[b]	0.801[b]	0.025[b]
	Curcumin 500 mg	-14.78 11.51)	-20.50--9.05			0.081[b]	0.783[b]
	Curcumin 1,000 mg	-12.22 (7.74)	-16.07--8.37				0.044[b]
	Negative control	2.5(-2 - 21)	2.07-9.92				
2 kHz	Positive control	-26 (8.79)	-30.36--21.63	<0.001[a]	0.570[b]	0.570[b]	<0.001[b]
	Curcumin 500 mg	-19(-29- 17)	-20.74--7.25			0.570[b]	0.005[b]
	Curcumin 1,000 mg	-20.83 (6.79)	-24.20--17.45				<0.001[b]
	Negative control	6.5 (6.56)	3.24-9.75				
3 kHz	Positive control	-6(-25 – 4)	-10.95--4.37	0.002[a]	0.003[b]	0.021[b]	0.031[b]
	Curcumin 500 mg	-1(-23 – 7)	-4.30- 2.30			1.000[b]	1.000[b]
	Curcumin 1,000 mg	-0.89 (6.69)	-4.21-2.44				<0.001[b]
	Negative control	-0.94 (8.08)	-4.96-3.07				
4 kHz	Positive control	-1.11 (8.48)	-5.32-3.10	0.125[c]			
	Curcumin 500 mg	2,28 (3,25)	0.66-3.89				
	Curcumin 1,000 mg	1,94 (5,06)	-0.57-4.45				
	Negative control	-2,39 (9,12)	-6.92-2.14				
5 kHz	Positive control	-3,78 (7,86)	-7.68-0.12	0.006[c]	0.029[d]	0.005[d]	0.001[d]
	Curcumin 500 mg	1,22 (4,75)	-1.13-3.58			0.505[d]	0.257[d]
	Curcumin 1,000 mg	2,73 (4,32)	0.57-4.87				0.639[d]
	Negative control	3,78 (8,79)	-0.59-8.14				
6 kHz	Positive control	-11,5 (5,29)	-14.1-- 8.86	<0.001[a]	0.010[b]	0.002[b]	<0.001[b]
	Curcumin 500 mg	-1,5 (-22 – 5)	-7.42--0.02			1.000[b]	0.408[b]
	Curcumin 1,000 mg	0 (-16 – 4)	-4.79-0.13				0.931[b]
	Negative control	1,39 (7,61)	-2.39-5.17				
7 kHz	Positive control	-8,94 (7,83)	-12.83--5.05	<0.001[c]	<0,001[d]	<0.001[d]	<0.001[d]
	Curcumin 500 mg	4,83 (6,97)	1.36-8.30			0.240[d]	0.408[d]
	Curcumin 1,000 mg	1,83 (7,76)	-2.02-5.69				0.118[d]
	Negative control	0,83 (7,77)	-3.03-4.69				
8 kHz	Positive control	-5,06 (7,98)	-9.02--1.08	<0.001[c]	<0.001[d]	<0.001[d]	0.005[d]
	Curcumin 500 mg	7,06 (5,36)	4.38-9.72			0.690[d]	0.005[d]
	Curcumin 1,000 mg	6,22 (6,05)	3.21-9.22				0.014[d]
	Negative control	0,94 (5,2)	-1.63-3.52				
9 kHz	Positive control	0,5 (7,09)	-3.02-4.02	<0.001[a]	0.123[b]	0.002[b]	0.403[b]
	Curcumin 500 mg	10 (-19 – 15)	1.23-11.09			1.000[b]	<0.001[b]
	Curcumin 1,000 mg	10,89 (4,83)	8.48-13.2				<0.001[b]
	Negative control	-7,11 (8,37)	-11.27--2.95				
10 kHz	Positive control	-12,28 (6,68)	-15.59--8.95	0.005[c]	0.001[d]	0,006[d]	0.087[d]
	Curcumin 500 mg	-3,56 (7,42)	-7.24-0.13			0.507[d]	0.083[d]
	Curcumin 1,000 mg	-5,22 (5,32)	-7.86- -2.57				0.280[d]
	Negative control	-7,94 (9,83)	-12.83--3.05				
11 kHz	Positive control	-14(-32 - -9)	-19.67--13.21	<0.001[a]	0.001[b]	0.016[b]	0.052[b]
	Curcumin 500 mg	-6,61 (9,44)	-11.30--1.91			1.000[b]	1.000[b]
	Curcumin 1,000 mg	-9,22 (5,6)	-12.00--6.43				1.000[b]
	Negative control	-11,17 (7,05)	-14.67--7.66				
12 kHz	Positive control	-20,78 (3,67)	-22.60--18.95	<0.001[a]	<0.001[b]	0.025[b]	0.001[b]
	Curcumin 500 mg	-9,78 (8,7)	-14.10--5.45			1.000[b]	1.000[b]
	Curcumin 1,000 mg	-13,28 (7,48)	-16.99--9.55				1.000[b]
	Negative control	-9,5(-32 - 0)	-16.6- -5.75				

Data were presented as mean (SD), median (min – max) [a]*Kruskal Wallis,* [b]*Dunn,* [c]*Oneway Anova,* [d]*Least Significant Difference (LSD)*

Table 5 showed that in the Curcumin 500 mg group, SNR values increased by 2.28 dB at 4 kHz, 1.22 dB at 5 kHz, 4.83 dB at 7 kHz, 7.06 dB at 8 kHz, and 10 dB at 9 kHz, with the highest increase at 9 kHz. In the 1,000 mg Curcumin group, SNR values increased by 1.94 dB at 4 kHz, 2.73 dB at 5 kHz, 1.83 dB at 7 kHz, 6.22 dB at 8 kHz, and 10.89 dB at 9 kHz, with the maximum increase also at 9 kHz.

Table 6. The Differences in HSP70 Levels Before and After Treatment

Group	Before Treatment		After Treatment		p*
	HSP70, pg/ml	95% Confidence Interval	HSP70, pg/ml	95% Confidence Interval	
Positive control	65.57 (27.14)	52.07-79.06	88.45 (30.89)	73.08-103.80	0.021
Curcumin 500 mg	58.97 (30.48)	43.81-74.12	65.82 (38.85)	46.49-85.13	0.523
Curcumin 1,000 mg	54.71 (28.89)	40.34-69.07	61.12 (36.55)	4.94-79.29	0.255
Negative control	33.20 (8.82)	28.81-37.58	32.92 (8.95)	28.47-37.37	0.834

Data were presented as mean (SD), pg/ml = picograms per milliliter **T Dependent*

Table 6 showed the increased HSP70 levels in the positive control and both Curcumin groups. No significant difference in HSP70 levels ($p>0.05$) was found between pre- and post-treatment in either Curcumin or negative control groups. Conversely, the positive control group showed a significant increase in HSP70 levels ($p=0.021$) between pre- and post-treatment.

Table 7. The Differences in Changes in HSP70 Levels Before and After Treatment

Group	HSP70, pg/mL	95% Confidence Interval	p*
Positive control	-22.88 (38.22)	-41.88- -3.87	0.102
Curcumin 500 mg	-6.85 (44.6)	-29.02-15.32	
Curcumin 1,000 mg	-6.40 (23.05)	-17.86-5.06	
Negative control	0.28 (5.54)	-2.47-3.03	

*Data were presented as mean (SD) *Kruskal Walllis*

Table 7 showed increased HSP70 levels in all experimental groups, with the highest increase in the positive control group (22.88 pg/mL). The Curcumin 500 mg group had a mean increase of 6.85 pg/mL, and the Curcumin 1,000 mg group had a mean increase of 6.40 pg/mL. The negative control group exhibited a worsening in HSP70 levels (0.28 pg/mL). Kruskal-Wallis test results indicated no significant differences in HSP70 levels among the groups ($p = 0.102$).

Discussion

In this study, male participants dominated the positive control, Curcumin 500 mg, and Curcumin 1,000 mg groups, comprising 88.9%, 83.3%, and 88.9% of the individuals, respectively. Subjects were selected from locations with noise levels exceeding 85 dB, including hospital laundry and nutrition facilities and an iron factory. Nyilo and Putri's study at Dr. Soetomo General Hospital, Surabaya, found that out of 48 workers with NIHL, 58.3% were female, and 68.75% worked in the Nutrition Installation (3). Ismail et al. reported that 49.7% of 173 workers in Kuching, Sarawak manufacturing facilities had NIHL, with males making up 75.7% of cases (17). Nurrokhmawati et al. observed that 56% of 66 employees in a Cimahi, Indonesia furniture factory had NIHL, with males comprising 95% of these cases (18). Men are more affected by workplace noise, likely due to greater exposure from job types, industries, and work histories, along with biological differences such as hormonal factors. Studies have indicated that women may have a natural defense against hearing loss, possibly linked to estrogen and its signaling pathways (19). Estrogen is vital for maintaining auditory function and protecting against age-related and noise-induced hearing loss in both sexes, mediated by estrogen

receptor β (ERβ). Studies have indicated that mice deficient in ERβ experience more severe cochlear hair cell damage and spiral ganglion injury after acoustic trauma (20). Workers with NIHL in our study had average ages of 37.11 years (control positive), 37.61 years (500 mg curcumin), and 37.78 years (1,000 mg curcumin), consistent with Nyarubelli et al., where 67.4% of Tanzanian iron and steel workers with NIHL were aged 18-35, and 26.2% were 36-43 (21). In 2002, approximately180,000 UK individuals aged 35-64 had severe hearing issues from workplace noise (5), with those aged 30-44 and 45-59 most vulnerable during their peak working years (19). The mean work duration was 13.17 years (positive control), 12.89 years (500 mg curcumin), and 12.17 years (1,000 mg curcumin), aligning with an Iranian study showing mild hearing impairment after 13.1 ± 7.8 years of service (22). Noise-induced hearing impairment advances rapidly in the first 10–15 years, then slows as the hearing threshold increases, unlike age-related hearing decline, which worsens progressively (23).

NIHL can be temporary or permanent (24). A permanent threshold shift is diagnosed when hearing loss persists after 14 days post-exposure, with recovery potentially extending to 30 days. A temporary threshold shift indicates a short-term reduction in hearing sensitivity, resolving within 24-48 hours. The sensory cells in the organ of Corti cannot regenerate after noise damage following repeated exposure, resulting in irreversible loss of nerve hair cells (5). PTA reveals that NIHL exhibits characteristic dips at frequencies of 3, 4, and/or 6 kHz, whilst maintaining normal hearing thresholds at 8 kHz (24). Due to outer ear resonance and middle ear mechanics, the 4 kHz region is particularly vulnerable to noise damage. Prolonged noise exposure can widen and deepen these notches, potentially affecting lower frequencies like 2, 1, and 0.5 kHz (25). Middle ear muscle reflexes protect against noise by contracting at frequencies of ≤ 2 kHz (5). High-frequency hearing loss is defined as a threshold shift of over 25 dB at frequencies ≥ 3 kHz with irregular audiogram results (26).

PTA showed a significant decline hearing threshold in the positive control group (p=0.001) post-treatment. The Curcumin 500 mg group significantly improved (p=0.046), whereas the Curcumin 1,000 mg and negative control groups showed no significant changes (p=0.059 and p=0.409).

No human studies have investigated the impact of curcumin on NIHL using PTA. Tajdini et al. examined diabetic patients with sudden hearing loss, revealed that combining intratympanic steroids with curcumin-piperine-gingerol supplements improved hearing more than steroids alone, according to PTA. The enhanced result is ascribed to the anti-inflammatory and antioxidant characteristics of curcumin, which contribute to a decrease in oxidative stress (27).

Currently, there is no existing research investigating the effects of curcumin administration on hearing function in workers with noise-induced hearing loss, as assessed by pure-tone audiometry, otoacoustic emissions (OAEs), and blood HSP70 levels, which are influenced by inflammatory processes.

A study conducted by Panahi et al. (2012) reported that administration of curcumin at a dose of 1,000 mg per day for four weeks reduced the severity of pruritus by decreasing the concentration of substance P, an indicator of inflammation, and by increasing the levels of superoxide dismutase, glutathione peroxidase, and catalase, all of which function as antioxidants in sulfur mustard–induced chronic pruritus (28). In this study, 500 mg Curcumin dose improved hearing thresholds more than a 1,000 mg dose, because Curcumin acts as a nutritional hormone with biphasic dose-response characteristics: low doses stimulate, while high doses inhibit and cause adverse reactions (29).

Before curcumin administration, a worsening in SNR was noted at 3-6 kHz in the positive control, 500 mg Curcumin, and 1,000 mg Curcumin groups. This supports Sliwinska et al.'s findings that industrial noise-induced hearing loss reduces DPOAE, especially at 3-4 kHz. Vinck et al. also observed a significant SNR worsening at 4 kHz post-noise exposure, with no full recovery despite PTA indicating no hearing loss at that frequency. OAE, particularly DPOAE at 4 kHz, is more sensitive than PTA for detecting early subclinical cochlear damage, a frequency that is highly vulnerable to NIHL (26).

The groups administered 500 mg and 1,000 mg Curcumin exhibited increased SNR values

at frequencies ranging from 4 kHz to 9 kHz, whereas the positive control group demonstrated reduced SNR values across all frequencies. The effects of curcumin on NIHL remain underexplored. Soyaliç et al. exposed animals to 110 dB noise for 8 hours and administered curcumin; OAE tests on days 1, 3, and 5 post-exposures showed stable DPOAE values at 3, 4, and 8 kHz, aligning with immunohistochemistry and histopathology findings. The curcumin group showed a slight increase in the apoptosis index of inner and outer hair cells compared to controls (30).

Yamaguchi et al. suggested that oral curcumin may protect against hearing loss from repeated sound exposure (31). Emekli et al. assessed mice with DPOAE tests pre-trauma, post-trauma, and 72 hours post-curcumin administration. The results indicated a significant SNR increase between the second and third tests and no significant SNR difference between the first and third assessments compared to the controls. The results suggest that curcumin may aid recovery after acoustic injury (32).

HSP70 in the plasma, resulting from danger signals or necrotic cell death, indicates noise-related damage (33).

Heat shock factor 1 (HSF1) regulates HSP gene transcription, which binds to HSP70 in the cytoplasm, detaches during stress to activate HSF1, then moves to the nucleus. Curcumin enhances HSP transcription and promotes cellular protection (34). A negative feedback mechanism involving HSP70 regulates the HSF1. Once HSP70 restores proteostasis, it reattaches to HSF1, deactivating it and completing the feedback loop (35).

HSP70 levels increased significantly ($p=0.021$) to a mean of 22.88 pg/mL in the positive control group. The groups administered Curcumin 500 mg and 1,000 mg also showed elevated HSP70 levels. No studies have examined the effect of curcumin on blood HSP70 levels in workers with NIHL. In noise-induced rats, Curcumin may prevent and treat cochlear lateral wall fibroblast damage by reducing HSP70 (36).

Silva et al.'s research on septic mice showed Curcumin significantly lowered plasma levels of pro-inflammatory cytokines IL-1β and IL-6 ($p<0.001$) and their concentrations in peritoneal lavage fluid ($p<0.05$), and serum HSP70 levels ($p<0.01$) (37). Changes in HSP70 levels are linked to various medical conditions, suggesting its potential as a disease biomarker. The mechanisms and accuracy are unclear, requiring extensive clinical trials for validation (38). HSP70 levels in the Curcumin 500 mg and 1,000 mg groups increased insignificantly compared to the positive control group, indicating adequate HSP70 production to restore proteostasis, deactivate HSF1, and complete the feedback cycle.

The limitations of this study included a relatively short intervention period of four weeks, a limited sample size, and potential residual confounding due to variations in occupational noise exposure, dietary antioxidant consumption, and other unmeasured lifestyle factors.

Consequently, the results should be regarded as preliminary indications rather than as providing definitive evidence.

Conclusion

In this short-term preliminary study, curcumin supplementation demonstrated a potential auditory benefit in noise-exposed workers, as evidenced by improved hearing threshold in the PTA examination, enhanced SNR at multiple frequencies, and reduced (albeit non-significant) SNR deterioration compared to the positive control group. Furthermore, blood HSP70 levels exhibited a non-significant elevation relative to the positive control. Longer-duration and larger randomized controlled trials are required to confirm the efficacy and elucidate the underlying biological mechanisms.

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